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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/533,613	01/30/2006	Richard G Vile	07039-444US1	6311

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EXAMINER	
HIRIYANNA, KELAGINAMANE T	
ART UNIT	PAPER NUMBER
1633	
MAIL DATE	DELIVERY MODE
05/31/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/533,613	VILE ET AL.	
	Examiner	Art Unit	
	Kelaginamane T. Hiriyanna	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,5,39 and 40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *2,5,39 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/06/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 03/06/2007 in response to office action mailed on 11/02/2006 has been acknowledged.

Claims 1, 3-4, and 6-38 are cancelled.

Claims 39-40 have been newly added.

Claims 2, 5, and 39-40 *are pending and are examined in this office action. Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is* ***571-273-8300.***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Claim Rejections - 35 USC § 103

Claims 2, 5 and 39-40 stand rejected under 35 USC § 103(a) as being unpatentable over Wang et al (1997, Cancer Res. 57:5426-33) in view of Liu et al (2000, Chinese Medical Journal 113:167-171) and Nowak et al., (2002, Seminars in Oncology 29:82-96).

The above claims are directed to a viral vector comprising a therapeutic polypeptide coding sequence that is operably linked to a heterologous destabilizing element wherein said heterologous destabilizing element is the 3' untranslated region of the TNF-α gene that enhances the expression of said polypeptide in target cells including tumor cells and in further limitation vector is an adenoviral vector or vaccinia virus vector.

Regarding claims 2, and 5, Wang teaches vector constructs wherein 3' UTR of the human TNF-α gene encompassing the mRNA destabilizing element was operably linked to luciferase reporter constructs and transfected into human breast carcinoma cell lines that over express TNF-alpha. The inserted 3' UTR markedly and quantitatively suppressed the luciferase activity. Increased levels of luciferase activity were observed 3 hr after TNF-alpha stimulation of ZR-75-1 cells transfected by constructs containing AU-rich repeats. Wang concludes that AU rich repeats in the 3'UTR of human TNF-α mRNA may regulate gene expression in human epithelial cancer cells (Abstract). Wang however, does not teach the use of nucleic acid encoding a therapeutic polypeptide and

use of Adenoviral and vaccinia viral vectors in generating constructs to express therapeutic genes in cells.

Liu teaches a viral vector used for transfecting murine breast tumor cells wherein IL2 gene, coding for a therapeutic polypeptide, is operably fused with TNF-alpha gene. The treated cells possessed lower tumorigenicity. Liu concludes the IL2-TNF-α fusion gene in concert act to improve their antitumor effectiveness.

Nowak teaches regarding using adenoviral vector and vaccinia viral vectors in making expression constructs for therapeutic genes for biologics, vaccines and genetherapy and other novel agents (Abstract). The therapeutic genes studied include tumor necrosis factor alpha (TNF-alpha) for treating malignant mesotheilioma (Abstract).

Thus it would have been obvious for one of ordinary skill in the art to modify the vector of Wang by substituting the luciferase gene with a therapeutic gene in view of Liu and Nowak and use the viral vectors including adenoviral and vaccine viral vectors as taught by Nowak wherein an operable fusion of TNF-α gene or its 3'UTR region with a heterologous gene coding for a therapeutic polypeptide and use the compositions for transducing cancer cells. One of skilled in the art would be motivated to do so as the 3'UTR elements of TNF-α selectively stabilize and modulate the expression of the therapeutic gene in a target cell as opposed to a non-target cell and hence can be used for enhanced expression of the therapeutic gene in a tumor cell. One of ordinary skill in the art would have reasonable expectation of success of making and using viral vectors with 3'UTR elements of tumor necrosis factor gene operably fused with a therapeutic gene in a adenoviral or vaccinia viral vector for treating tumor because of the teachings in the art. Thus, the claimed invention was *prima facie* obvious.

Response to Argument of 03/06/2007:

Applicant argues that at no point does the combination of Wang reference and Liu reference suggest that a person having ordinary skill in the art should replace the luciferase gene in the vector disclosed in Wang et al. reference with any other nucleic acid, let alone a nucleic acid encoding a therapeutic polypeptide and hence the cited combination of art does not make the invention obvious.

However, this argument is found not persuasive because Wand clearly teaches that the inserted 3' UTR of TNF-alpha gene markedly and quantitatively suppressed the luciferase activity. Increased levels of luciferase activity were observed 3 hr after TNF-alpha stimulation of ZR-75-1 cells transfected by constructs containing AU-rich repeats. Further it is standard practice in the art first to test the control/regulatory sequences (here 3' UTR of TNF-alpha gene) using a marker or reporter gene before incorporating a therapeutic gene. Thus, the results of expression of a marker gene in said construct

anticipates the expression of a substituted therapeutic gene or any gene of interest in its place and this concept is routinely practiced in the art. Thus the combination of the art cited makes the instantly claimed invention obvious. Hence the rejection is reapplied.

Conclusion:

No claim allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Kelaginamane Hiriyanna* whose telephone number is **(571) 272-3307**. The examiner can normally be reached Monday through Friday from 9 AM-5PM. Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst *William N. Phillips* whose telephone number is ***571 272-0548.*** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Joseph Woitach*, may be reached at **(571) 272-0739.** The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). When calling please have your application serial number or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. For all other customer support, please call the USPTO call center (UCC) at (800) 786-9199.

Kelaginamane T. Hiriyanna
Patent Examiner
Art Unit 1633

SUMESH KAUSHAL, PH.D.
PRIMARY EXAMINER